

## Case report

### MINOXIDIL OVERDOSAGE: A CASE REPORT

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#### Abstract

A 64-year-old man ingested about 60 ml 2% of topical minoxidil solution in order to make his hair grow faster. Twelve hours after ingestion he was brought to the University Clinic of Toxicology with severe hypotension, tachycardia, chest pain and subendocardial ischemia. ECG showed diffuse T-wave inversion and depressed ST segments. He was also oligoanuric at admission. In spite of the intensive hydration with crystalloid solutions and intravenous dopamine administration that resulted in partial hemodynamic improvement and resolution of the ECG changes, kidney failure occurred. After two hemodialysis sessions, urea and creatinine levels returned to normal and rebound hypertension appeared. The patient was discharged after 12 days of hospitalization in a good condition. Topical minoxidil solution is formulation used for treatment of androgenic alopecia. If orally ingested it leads to severe hypotension, acute coronary syndrome, compensatory tachycardia and acute kidney failure. Emergency therapeutic approach is a precondition for successful outcome.

**Keywords:** minoxidil, dopamine, subendocardial ischemia.

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#### Introduction

Minoxidil is a known antihypertensive drug, which has recently been approved for treatment of androgenic alopecia. It can be found on the market as 5% and 2% solution. Sixty ml of 2% solution contains about 1,200 mg of minoxidil, which is approximately 12 times greater than the maximum recommended daily dose for controlling hypertension. Correlation between minoxidil in

gestion and development of subendocardial ischemia, hemodynamic impairment and acute kidney failure (AKF) will be discussed in this paper.

#### Case report

A 64-year-old man with no prior history of kidney failure and cardiologic diseases was brought as an emergency case into the University Clinic of Toxicology 12 hours post-ingestion of 60 ml 2% of minoxidil solution (Pilfud, Bosnalijek). He ingested the solution in order to achieve rapid therapeutic effects. He denied use of alcohol or other medications, but said he suffered from a moderate hypertension. On admission he was conscious, oriented to time and place, afebrile, eupneic. His pulse was 110/min, and blood pressure was 60/20 mmHg. The patient experienced chest pain, epigastric discomfort, weakness and malaise. ECG showed tachycardia and signs of subendocardial ischemia. Therapy was initiated with resuscitation with 2.5 liter of physiological solution given in the first 7 hours, but the patient was anuric. Following administration of 8 mcg/kg/min dopamine the blood pressure increased to 90/60 mmHg at 12 hours after admission, and at 24 hours it reached and remained at 100/70 mmHg in the first three days. The dose of dopamine was gradually reduced to 2 mcg/kg and discontinued after 48 hours. Diuresis was 100/300/700 ml/24 hours on the first/second/third day, respectively, but the values of degradation products increased. The

Table 1. The most characteristic laboratory and clinical parameters

day	hours	CK	CK-MB	CK-MB%	Na	K	urea	creatinine	diuresis/24h	TA
1	09	346	19	5.49	136	4.2	11.1	310	100	60/20
	21	992	14	1.41	141	4.0	15.1	356		90/60
2	09	1098	52	4.74	138	4.8	28.6	601	250	100/70
	21	720	45	6.25	136	4.5		659		90/50
							31.9			
3	09	324	22	6.79	134	4.4	34.6	625	700	90/50
	21				128	4.3	36.5	757*		100/60
4	09	200	14	7.00	134	4.5	21.6	270*	2000	150/85
7	09	170	10	5.88	139	4.8	14.9	124	6400	180/100
10	09	84	8	9.52	140	4.4	4.5	74	9100	200/130
	21									170/110
12	09	75	6	8.00	142	4.5	5.0	82	3000	140/90
	21									130/80

Values of CK, CK-MB, urea, creatinine are expressed in mmol/l, diuresis in ml/24h, blood pressure in mm Hg. \*hemodialysis

patient underwent two hemodialysis sessions on the third and fourth day, which resulted in a polyuric phase and decrease of urea and creatinine. Blood pressure started to increase and since the fourth day until the end of the hospital stay ranged from 150/85 to 200/130 mmHg (rebound hypertension).

Laboratory analysis showed leukocytosis, increase of CK (creatine kinase) and CK-MB, which did not surpass 10% of the CK value, and troponine was negative. Urea and creatinine peaked at 36.5 mmol/l and 757 mmol/l, respectively, on the third day and returned to normal on the 10th day. The remaining laboratory findings were unspecific (Table 1).

The first day ECG revealed diffusely inverted T-waves with depressed ST segments in V2-V6. These changes withdrew and ECG stabilized on the third day (Figure 1, Figure 2).

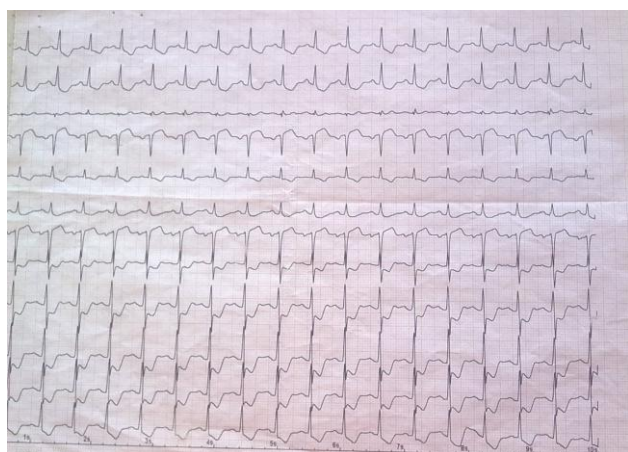


Fig.1. First day ECG

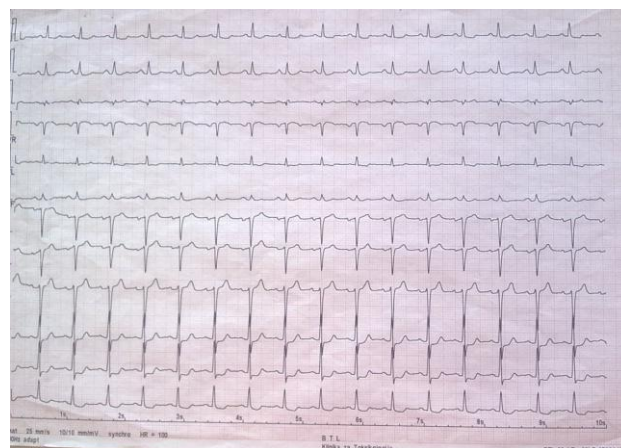


Fig. 2. Third day ECG

## Discussion

Minoxidil, which was originally used for treatment of hypertension, recently has been approved for treatment of male pattern baldness [1]. Adverse effects of minoxidil local application are rare and minor. Most commonly it can cause itching and irritation on the affected area and other dermatologic complications and minor systemic effects due to its small resorption. The systemic application of minoxidil is associated with more serious complications.

Minoxidil is activated in the liver and its action is to relax vascular smooth muscle by opening cell surface potassium channels causing an efflux of potassium, hyperpolarization and relaxation of smooth muscle cells. Minoxidil produces systemic hypotension by a direct arteriolar vasodilatation and is associated with a reflex

increase in cardiac output and myocardial contractility mediated by the sympathetic nervous system. Maximal concentration in the blood is achieved 1 hour after oral administration, but due to delay of active metabolic for-

mation, the maximal therapeutic effect appears much later. The serum half-life is 3 to 4 hours, but the effect can last 24 hours or longer [2]. Minoxidil is eliminated mainly by hepatic metabolism.

There are reports that minoxidil does not cause hypotension in normotensive individuals [3]. However, many authors report prolonged hypotension post-ingestion, which lasts two to four days after admission to the hospital [4,5].

Various cardiovascular manifestations resulting from different doses of minoxidil have been reported. Lower doses produce hypotension and successive increase in doses leads to tachycardia and myocardial ischemia. This tachycardia and resultant myocardial ischemia are probably a compensatory mechanism for severe hypotension. These cases are treated with combination of crystalloids, dopamine [6] and phenylephrine infusion [7] guided by the cardiovascular parameters.

The greater the contractility, the more oxygen the myocardium consumes. Increased heart rate (HR) leads to increased myocardial O<sub>2</sub> consumption.

In our patient, in addition to prolonged hypotension and tachycardia coronary syndrome developed along with reverse ECG changes and negative CK-MB and troponine. Subendocardial ischemia is believed to be caused by an increased myocardial oxygen demand due to secondary catecholamine overload that increases myocardial contractility and decreased coronary perfusion that is due to tachycardia and hypotension acute minoxidil intoxication. Similar transitory ECG changes when larger doses of minoxidil (about 3 grams) had been given were described by other authors [8,9]. Some authors have presented development of nontransmural infarction as a result of ingestion of similar amount of minoxidil solution, associated with pleural effusion and good response to conservative treatment [7].

Besides coronary syndrome, the patient developed AKF that did not respond to the conservative treatment, but hemodialysis was required for returning the degradation products to normal values. In our patient the cause for kidney failure was dishemodynamic and was probably a result of delayed hospitalization (12 hours post-ingestion) and prolonged kidney hypoperfusion. In other case reports a smaller degree of oliguria was registered as well as a smaller increase in degradation products with more rapid response to drug treatment as a result of the urgent hospitalization (two hours post-ingestion at the most) [5,7,9]. There is a lack of literature on minoxidil direct nephrotoxicity that results in decreased kidney function in a state of acute overdosage. Therefore, we assume there was a prerenal failure in our patient, which was caused by hemodynamic insufficiency and suffered renal hypoxia.

The so-called rebound hypertension was registered in our patient, which appeared on the 4<sup>th</sup> day of the hospital stay, that is, following hemodialysis and establishment of diuresis.

By definition rebound hypertension is an increase in blood pressure in response to stopping or reducing high blood pressure medication. Severe cases can result in a very large increase in blood pressure which requires prompt treatment to avoid complications such as organ damage. Hypertension in our patient was a result of blood pressure establishing without therapy, when minoxidil, which is dialyzable, was completely eliminated and kidney function was improved. Although prazosin was included in the therapy on the seventh day, peak value was reached on the 10<sup>th</sup> day of hospitalization (200/130 mmHg), and it returned to normal until the discharge day by dose adjustment of prazosin in the therapy. There are no case reports in the literature presenting with rebound hypertension after minoxidil intoxication. However, this phenomenon has been described in children treated with several hypertensive drugs after discontinuation of minoxidil therapy due to the development of hypertrichosis. Rebound hypertension was manifested with hypertensive encephalopathy in those children in whom minoxidil was withdrawn rapidly. The occurrence of rebound hypertension correlated well with the cumulative dose of minoxidil and the rapidity with which minoxidil was withdrawn [10]. Thus, we think this phenomenon can appear also in patients intoxicated with minoxidil, who had a history of hypertension and can be an additional risk factor for onset of other co-morbidities if it is not expected and not treated.

In summary, we have presented a case of severe poisoning after ingestion of 2% of topical minoxidil solution. This is the first case in our clinical practice, which was manifested with severe hypotension, tachycardia, subendocardial ischemia, AKF and rebound hypertension. As the use and availability of these solutions for local application is increasing, a greater awareness of systemic toxic effect of minoxidil is also necessary as well as immediate and adequate treatment.

*Conflict of interest statement.* None declared.

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